Non-invasive, real-time biosensing of physiologic hydration status via ultra-compact, laser-based short-wave infrared spectrophotometry

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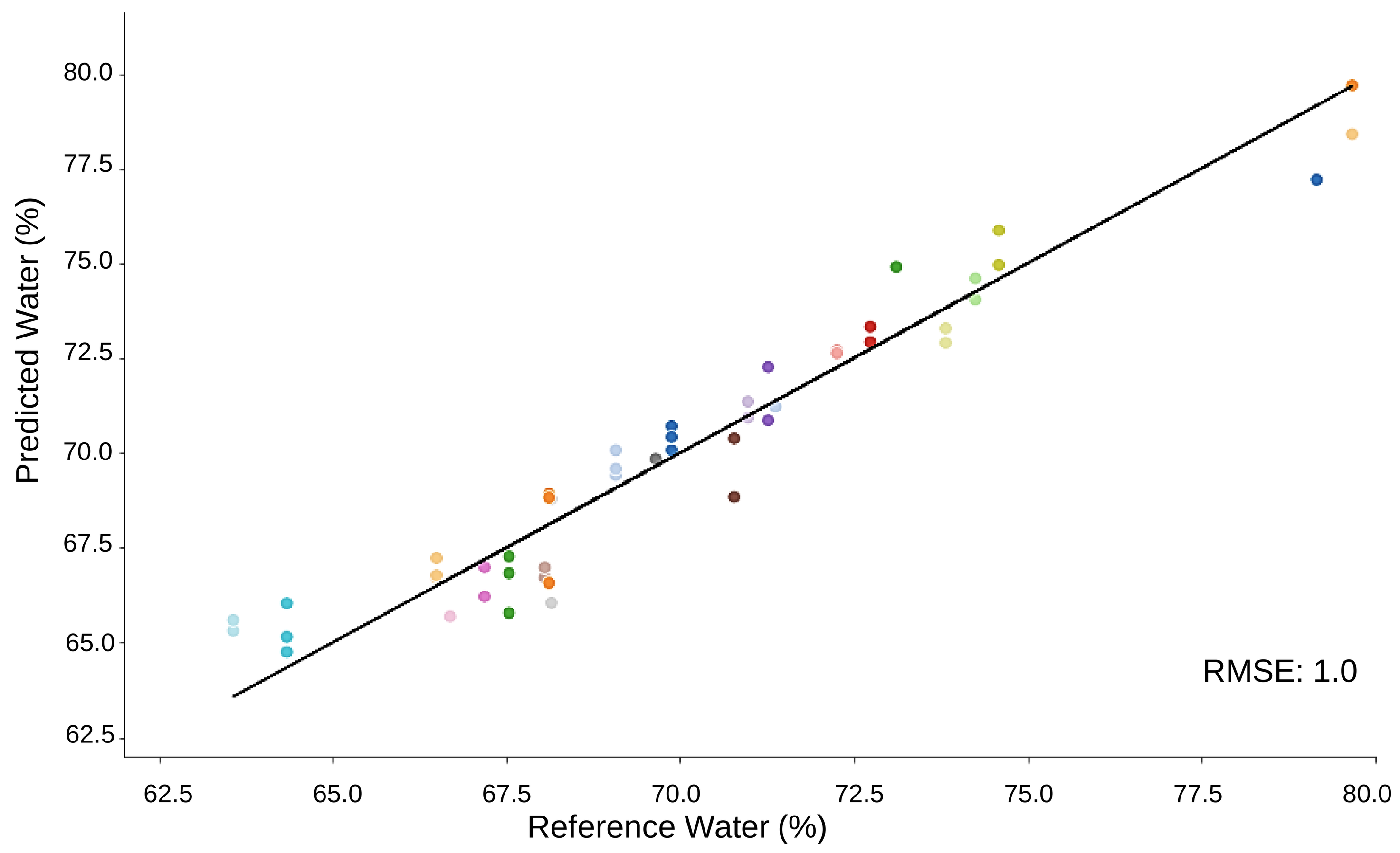
INTRODUCTION

The ability to optically derive an individual's dermal water concentration continuously and non-invasively, has potential to satisfy a large, unmet need in the defense, wellness and healthcare industries. We report on the the integration of a silicon-based photonics integrated circuit (PIC) containing more than 30 individual laser diodes into a wearable form factor, allowing for the identification of water-based spectral signatures specifically in the 1200-1800 nm short-wave infrared (SWIR) region. The derived application gives insight into total body water levels, translating to hydration.

Preliminary Tissue Phantom Study Results



Phantom composition: gelatin, intralipids and predetermined percentage of water ranging from 63.5-79.6%; n=25 phantom cuvettes; measurements taken in triplicate using a Gen A benchtop system.

APPLICATION. By denoting a change in the absorbance of water molecules in the interstitial fluid within the dermis, a model may be developed that derives physiologic hydration status in generally healthy adults. The derivative application is advantageous over other common technologies and tests, which may present clear limitations in validity, cost, or an inability to monitor trends longitudinally on continuous basis. Further, real-time data collection and delivery penetrates use cases such as dehydration monitoring in vulnerable and high-risk populations, including military operations.

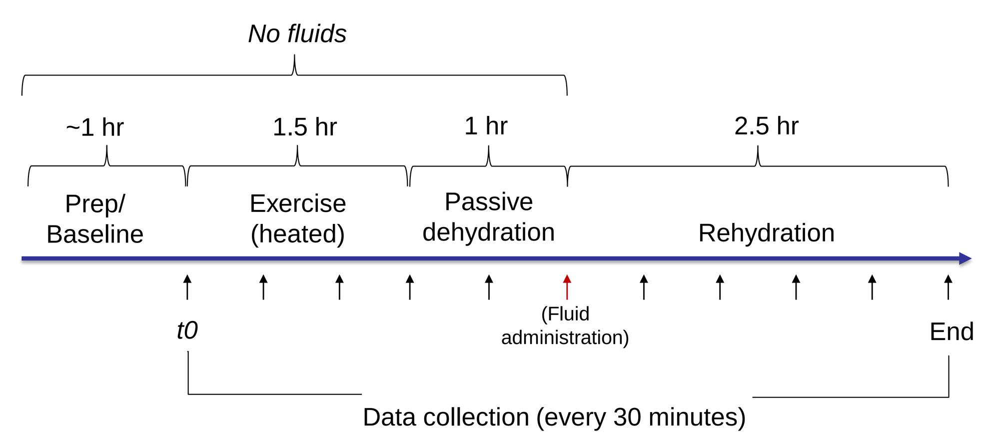
After completing a study using synthetic tissue phantoms, follow on in vivo studies were warranted. It was hypothesized that data collected using a wearable, laser-based SWIR spectrophotometric sensor during temperature- and humidity-controlled exercise and sauna treatments would result in a predictive model that can successfully delineate between clinically-indicated euhydration, underhydration and mild dehydration.

METHODS

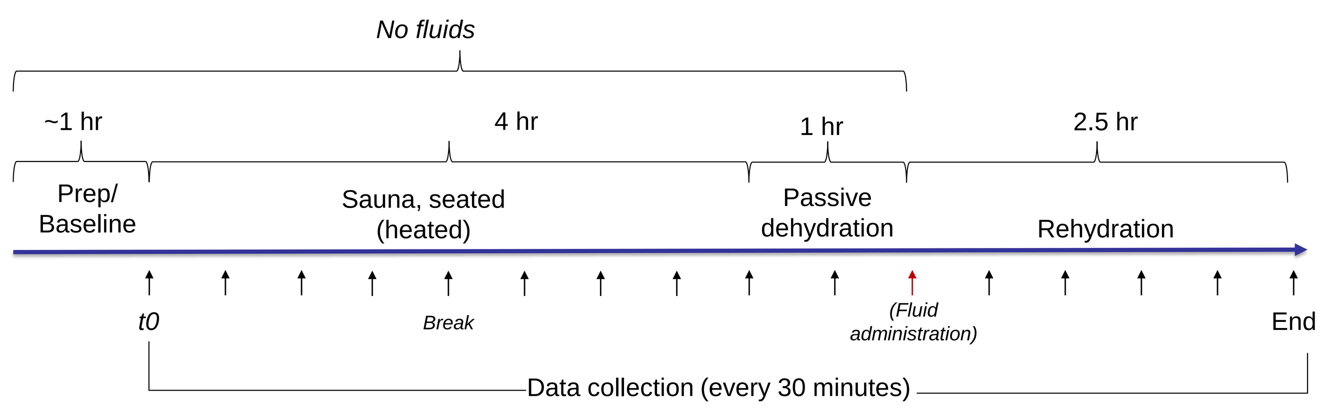
Exercise protocol: Investigational wrist-based wearable devices were emplaced on heathy, active adults, with sensors on the central zone of the dorsal wrist. Subjects were instructed to hydrate the evening prior and morning of, ceasing fluid ingestion 2.5 hours prior to lab arrival. First morning urine and baseline data were collected [urine osmolality (UO) and specific gravity (USG), nude body mass (BM), body composition, serum osmolality, sodium and glucose, SWIR and PPG spectra, whole-body infrared thermal imaging, skin and core temperature). Moderate-intensity exercise was conducted for 90 min on a cycle ergometer in a heated chamber [100-105 ° F (37.8-40.6 ° C); 35-50% humidity]. Postexercise, subjects remained semi-supine in ambient conditions for 1 hr. They were given 1 L of hypertonic solution (Liquid IV) to drink ad libitum, and monitored for an additional 2.5 hours. Physiologic data was collected every 30 min for the duration of the protocol. SWIR spectra and core temp were collected continuously.

Sauna protocol: Subjects were instructed as above; in place of exercise, subjects remained seated in a heated chamber [100-105 ° F (37.8-40.6 ° C); 35-50% humidity] for 4 hrs, with break at the 2 hr mark.

Exercise Protocol Diagram



Sauna Protocol Diagram



RESULTS

Rockley ETM device (left).

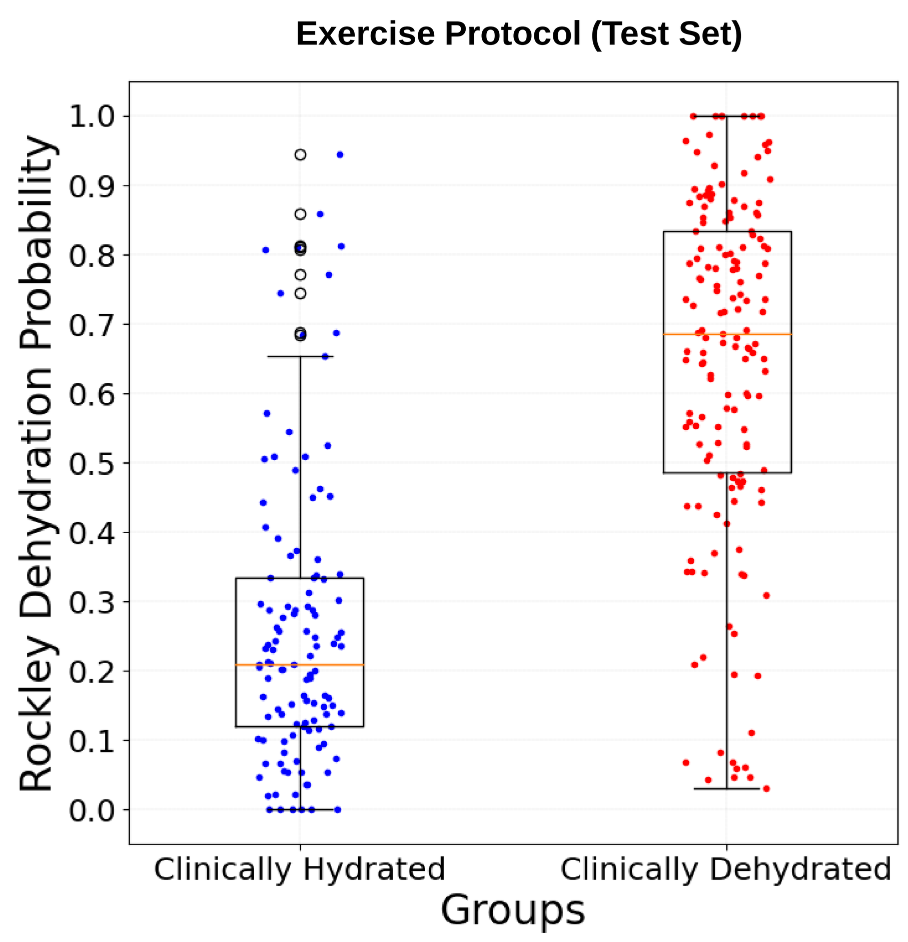
A PCA components + logistics regression model was created using ETM spectra (right) and validated against normal clinical values for BM changes, USG and UO to classify euhydration and mild dehydration.

- *Clinically dehydrated* defined as BM loss ≥2%, USG ≥1.020, and UO ≥775 mOsm/kg, respectively.

Preliminary alpha device results (below) had the addition of a third classifier (underhydrated):

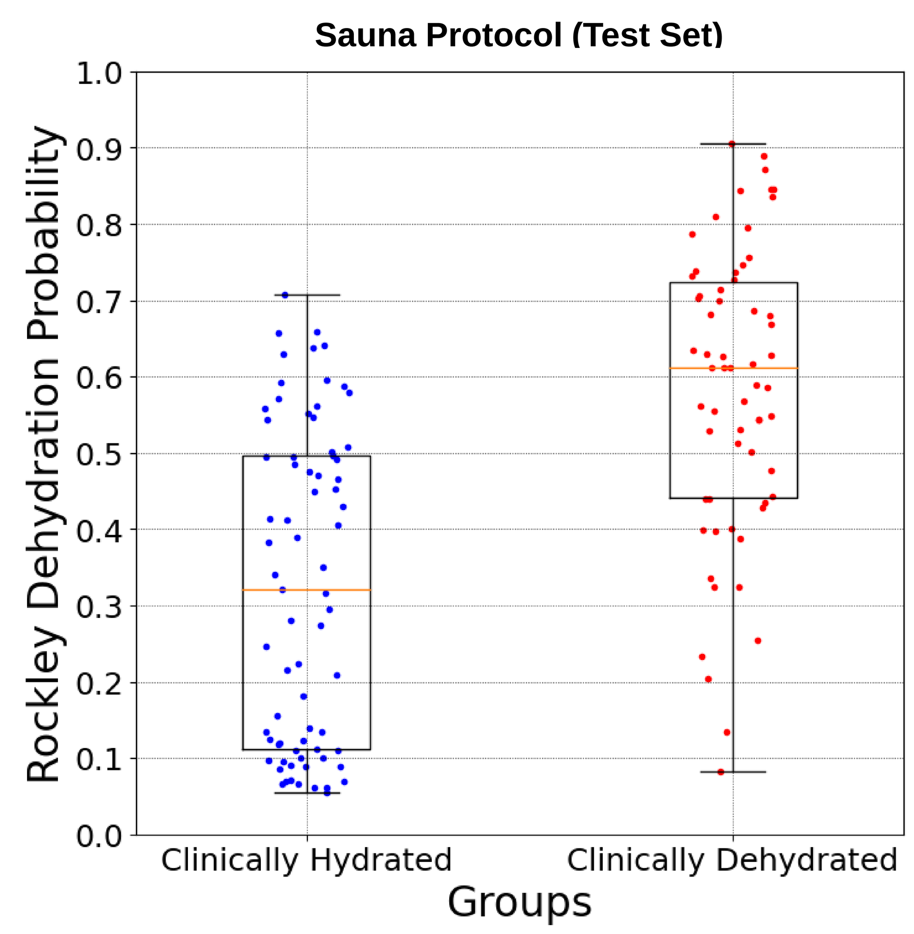
- BM loss was at least 1% but <2%; USG was 1.105 but <1.020, UO was between 625 but <775 mOsm/kg.

ETM Device Results



Data compares hydrated session (baseline) against the end of the postexercise passive dehydration session; n=13. Results for test set (n=4):

- *AUC: 0.86*
- *Sensitivity: 0.80*
- *Specificity: 0.84*
- *Hydrated records: 117*
- *Dehydrated records: 155*



Data compares hydrated session (baseline) against the end of the passive dehydration session post-treatment; n=16. Test set: n=4.

- *AUC: 0.81*
- *Sensitivity: 0.73*
- *Specificity: 0.63*
- *Hydrated records: 73*
- *Dehydrated records: 62*

Rockley Bioptx™ Band Alpha device.

Preliminary Alpha Device Confusion Matrix

Test Data	Pred-Eu	Pred-Un	Pred-De	Norm-Acc
Eu	0.71	0.33	0.19	0.49
Un	0.12	0.15	0.20	
De	0.17	0.53	0.61	

Eu=Euhydrated; Un=Underhydrated; De=Mild Dehydration;
The predictive accuracy for determining if a subject was euhydrated was 71%; Accuracy for dehydration was 61%.

CONCLUSIONS

Integration of ultra-compact SWIR-based spectrophotometry into a non-invasive wearable device may detect clinically-useful changes in body water status during acute and prolonged periods of active water loss or gain.

Improvements in hardware stability and indexing will lead to more precise delineations between physiologic changes in dermal water concentration. Real-time, predictive capturing of an underhydrated state (1-<2% body mass loss) is favorable in attempting to prevent the onset of a dehydrated state. Index developments may lead to increased utility in use cases that require insight if a user is overhydrated or at risk for moderate to severe dehydration, such as military personnel during field operations and in extreme environments, casualty care, as well use cases such as elder care and fitness/athletics hydration optimization.

REFERENCES

1. Agache, P., & Humbert, P. (2004). Measuring the skin. Springer Science & Business Media.
2. Armstrong, L. E., Johnson, E. C., McKenzie, A. L., & Munoz, C. X. (2013). Interpreting common hydration biomarkers on the basis of solute and water excretion. European journal of clinical nutrition, 67(3), 249-253.
3. Heitz, U., & Horne, M. M. (2012). Pocket Guide to Fluid, Electrolyte, and Acid-Base Balance-E-Book. Elsevier Health Sciences.
4. Nose, H., Mack, G. W., Shi, X., & Nadel, E. R. (1994). Ch 11, Shift in body fluid compartments after dehydration in humans. Institute of Medicine (US) Committee on Military Nutrition Research; Marriott BM, editor. Fluid Replacement and Heat Stress. Washington (DC): National Academies Press (US)
5. Péronnet, F., et al. (2012). Pharmacokinetic analysis of absorption, distribution and disappearance of ingested water labeled with D2O in humans. European journal of applied physiology, 112(6), 2213-2222.